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Temporal Trends in the Quality of Deceased Donor Kidneys and Kidney Transplant Outcomes in Europe: an analysis by the ERA-EDTA Registry

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Running title: Temporal Trends in Deceased Donor Kidney Quality

ABSTRACT

Background. We investigated ten-year trends in deceased donor kidney quality expressed as the kidney donor risk index (KDRI) and subsequent effects on survival outcomes in a European transplant population.

Methods. Time trends in the crude and standardised KDRI between 2005-2015, by recipient age, sex, diabetic status, and country were examined in 24,177 adult kidney transplant recipients in seven European countries. We determined five-year patient and graft survival probabilities and the risk of death and graft loss by transplant cohort (cohort 1: 2005-2006, cohort 2: 2007-2008, cohort 3: 2009-2010) and KDRI quintile.

Results. The median crude KDRI increased by 1.3% annually from 1.31 (interquartile range, IQR: 1.08-1.63) in 2005 to 1.47 (IQR: 1.16-1.90) in 2015. This increase i.e., lower kidney quality, was driven predominantly by increases in donor age, hypertension and donation after circulatory death. With time, the gap between the median standardised KDRI in the youngest (18-44 years) and eldest (>65 years) recipients widened. There was no difference in the median standardised KDRI by recipient sex. The median standardised KDRI was highest in Austria, the Netherlands, and Basque Country (Spain). Within each transplant cohort, the 5-year patient and graft survival probability were higher for the lowest KDRIs. There was no difference in the patient and graft survival outcomes across transplant cohorts, however over time the survival probabilities for the highest KDRIs improved.

Conclusions. The overall quality of deceased donor kidneys transplanted between 2005-2015 has decreased and varies between age groups and countries. Overall patient and graft outcomes remain unchanged.

Keywords: deceased donors, epidemiology, survival outcomes, transplantation

KEY LEARNING POINTS

What is already known about this subject?

Deceased donor kidneys with higher KDRI scores have worse survival outcomes than those with lower KDRI scores. To meet demands, older and more marginal kidneys are being used. It is not known if the increased use of marginal kidneys has resulted in worse transplant outcomes over time.

What this study adds?

Over a ten-year period, transplant recipients over 45 years old have received kidneys with increasingly higher KDRIs i.e., worse quality. These kidneys are increasingly coming from donors that are older, more likely to have a diagnosis of hypertension and retrieved from donors after circulatory death, though this varied between countries. This has not translated to poorer five-year kidney transplant outcomes.

What impact this may have on practice or policy?

As life expectancy in the general population increases, and the prevalence of diabetes mellitus, hypertension and obesity increases it is likely that we will continue to see poorer quality donor kidneys. To avoid this translating into worse kidney transplant outcomes the transplant community should focus on identifying therapies and/or preventative strategies aimed at improving kidney transplant outcomes despite these lower quality allografts.

INTRODUCTION

In order to meet the demand of kidneys for transplantation, which continues to exceed the current supply (1, 2), an increasing number of marginal kidneys are being utilised (3, 4). Marginal kidneys have been associated with worse graft survival outcomes (5). The kidney donor risk index (KDRI), derived from ten deceased donor factors, provides an estimate of how long a deceased donor kidney allograft can be expected to function for, relative to 'the median' deceased donor kidney retrieved in the United States (US) in the previous calendar year (6). The KDRI has now been validated in several European countries (7-9). Lower KDRI scores represent a higher estimated graft survival time, whereas higher KDRI scores represent a lower estimated graft survival time (10). A deceased kidney donor in 2017 with a standardised KDRI score of 1.5 equates to a 1.5 times higher relative risk of allograft failure compared to the 'median' deceased donor kidney from 2016. Given that the KDRI is standardised to the median donor of the previous year, the reference group is changing on an annual basis, and, as a consequence, a donor represented by a KDRI of 1.5 in one year, may not be same as a donor represented by a KDRI of 1.5 in previous years. By standardising the KDRI over a number of years to the same reference donor, i.e. the median deceased donor in one chosen year, one has a quantitative measure with which to assess the quality of deceased donor kidneys in a given population and across populations over time.

Using data from kidney and transplant registries in seven European countries we investigated the trends in the quality of transplanted deceased donor kidneys between 2005 and 2015, expressed as KDRI scores, and standardised to a reference KDRI score. We identified annual trends in standardised KDRI scores over a ten-year period by recipient sex, recipient age group, recipient diabetic status, and country of transplantation. Furthermore, we assessed patient and graft survival outcomes by KDRI quintile over time.

MATERIALS AND METHODS

Data collection

Data from the ERA-EDTA Registry with additional data collection from nine individual kidney and transplant registries in seven countries were used; Austrian dialysis and transplant registry, Eurotransplant, Danish Nephrology Registry, Scandiatransplant, Information unit about renal patients from the Basque Country, Dutch Transplant Foundation, Norwegian Renal Registry, Slovenian Renal Registry and United Kingdom Transplant Registry held by NHS Blood & Transplant. The recipients included in the study were restricted to those aged ≥18 years at the time of first, kidney only, ABO-compatible transplants performed during 1st January 2005 to 31st December 2015. No data were collected regarding deceased donors from whom kidneys were subsequently not recovered or discarded once recovered. All national and regional kidney registries contributing data to the ERA-EDTA Registry followed their national legislation regarding ethics committee approval.

Data analysis

Missing data

Overall, 80% of cases had complete donor details except for donor ethnicity and hepatitis C (HCV) status (Supplemental Table 1a and 1b). Where the donor ethnicity and HCV status were unavailable, we assumed that, in this European setting, the donor was Caucasian and HCV negative. Based on the differences between the complete cases and the cases with missing variables, it was concluded that with the exception of donor diabetes and hypertension in Norway, the data was missing completely at random, therefore the missing variables were imputed in SAS using the multiple imputation procedure (proc mi). The donor variables included in the imputation model were donor age, height, weight, prior diagnosis of hypertension, prior diagnosis of diabetes mellitus, creatinine, cause of death and donor type (donation after circulatory death [DCD] or donation after brain death [DBD]).

Five imputed datasets were created. Log transformations were used for non-normally distributed data, which were then transformed back to their original form before the analysis (11). Missing variables were imputed by country for example only donor and recipient data from Austria was used to impute Austria's missing data.

Evaluating time trends in the KDRI

Using the donor characteristics and the KDRI beta coefficients as determined by Rao et al (6) we calculated the 'donor-only' KDRI for each individual donor (Box 1). We then determined the distribution of the crude KDRI for the years 2005, 2010 and 2015, overall and by recipient sex, recipient age group (18-44, 45-54, 55-64, ≥65 years), recipient diabetic status and country. These data were presented as violin plots which have the advantages of both box plots, thereby allowing the visualisation of summary statistics, and density traces, thereby allowing visualisation of the data distribution.

We examined for time trends in KDRI between 2005 and 2015. To have a meaningful comparison of the KDRI over time, a scaling factor was applied. In these analyses for all the years in question, we used the median KDRI from 2005 as the scaling factor, thereby giving the 2005 median KDRI of the whole group a score of 1. The same groups as for the distribution of the crude KDRI were examined, i.e.

1. All countries/regions combined: overall and by recipient sex, recipient age group, and recipient diabetic status.
2. Time trends in the individual countries/regions.

Time trends in the standardised KDRI were examined using Joinpoint regression (12). The year was taken as the explanatory variable and the scaled median KDRI as the outcome. The average annual percentage change (AAPC) was computed using Poisson regression as provided by the Joinpoint regression program (13).

Survival analysis

Kaplan-Meier and Cox Regression were used to calculate five-year patient and graft survival probabilities and the risk of death and graft loss respectively by transplant cohort and by KDRI. To allow for analysis of five-year follow up, the recipients were divided into three transplant cohorts; cohort 1: 2005-2006; cohort 2: 2007-2008; and cohort 3: 2009-2010. Thereafter the cohorts were further subdivided by KDRI quintiles, which had been standardised to the median 2005 KDRI. The KDRI quintiles were 0.45-<0.79; 0.79-<0.96; 0.96-<1.15; 1.15-<1.45; ≥1.45. The date of transplantation was taken as the starting point, and the patients were followed until the event of interest. For patient survival the event of interest was death. For graft failure, the events of interest were either a return to dialysis, re-transplantation, or death with a functioning allograft. Patients were censored for loss to follow-up and the end of the study period was set as the 31st December 2015. In the adjusted analysis, we adjusted for recipient age at transplantation, recipient sex, primary kidney diagnosis, cold ischaemia time (CIT), human leukocyte antigen (HLA) mismatch score, and country of transplantation.

Sensitivity analysis

A sensitivity analysis of complete cases i.e., only cases where all donor variables except for donor HCV status and ethnicity were available was performed. To account for the increasing number of DCD transplants over time, the crude and standardised KDRI scores for DBD transplants were calculated.

A two-tailed p-value of <0.05 was considered statistically significant. Analyses were performed using SAS software version 9.4 and Joinpoint 4.0.4 (14).

RESULTS

We included 24,177 recipients, transplanted between 2005 and 2015. During this period the median recipient age rose from 53 (interquartile range, IQR: 43.0-61.5) to 55 years (IQR: 45.0-65.0) and the percentage of recipients with a diagnosis of diabetes mellitus rose from 12.5% to 17.0%. The median deceased kidney donor age rose from 50 years (IQR: 38-59) in 2005 to 55 (IQR: 44-65) in 2015 (Table 1). The percentage of donors with a history of hypertension (23% to 30%), diabetes mellitus (4% to 8%), and severe obesity (body mass index >35 kg/m^2; 4% to 7%) increased.

Trends in crude KDRI

For all countries combined, the median crude KDRI was 1.31 (IQR: 1.08-1.63), 1.41 (IQR: 1.13-1.81), and 1.47 (IQR: 1.16-1.90) in 2005, 2010 and 2015, respectively (Figure 1 top left). The median crude KDRIs presented for all countries combined can be found in Figure 1 and Supplemental Table 2, and by individual country can be found in Supplemental Figure 1 and Supplemental Table 2.

Trends in standardised KDRI

When standardised to the median KDRI from the total group in 2005 one can objectively visualise annual changes in the 'median donor' based on ten deceased donor factors. Between 2005 and 2015 this standardised median donor KDRI increased from 1.00 to 1.13, giving an average annual percentage change of 1.3% (95%CI: 0.6-2.0, Figure 2a, Supplementary Table 3). The standardised median donor KDRI increased for both female and male recipients by an average annual percentage change of 1.5% (95%CI: 1.0-2.0) and by 1.2% (95%CI: 0.8-1.6) respectively, with no differences between the sexes (p=0.851, Figure 2b). There appeared to be a trend towards a decline in the standardised median KDRI for the recipients aged 18-44 (AAPC -0.3%, 95%CI: -0.6-2.3). Over time the gap between the standardised KDRI in the youngest and oldest recipients widened. The standardised median KDRI in 2015 for recipients aged 18-44 was 0.89 whereas for recipients ≥65 years it was 1.48

(Figure 2c, Supplementary Table 3). Recipients with diabetes mellitus remained in receipt of lower quality donor kidneys compared to recipients without diabetes mellitus throughout the 10-year period ($p<0.001$), though the KDRI increased for both diabetic and non-diabetic recipient groups (Figure 2d, Supplementary Table 3).

Overall Austria, Basque Country (Spain), and the Netherlands had higher annual standardised median KDRIs than Norway and Slovenia (Figure 3, Supplementary Table 3). Austria, Basque Country (Spain), and the Netherlands continued to have higher than average standardised KDRIs when recipients were stratified by older age (Supplemental Figure 2). The driving factors behind these differences varied by country (Table 2). The high standardised KDRI in Austria, Basque Country (Spain), and the Netherlands was mainly driven by a higher proportion of deceased donors aged >50 years and donors with a diagnosis of diabetes mellitus. In addition, within the Netherlands and the UK almost 50% of donors were DCD donors, whilst they only made up 5% of donors in Norway and 0% of donors in Slovenia and Denmark.

Survival analysis was performed on 11,767 first transplant recipients transplanted between 2005-2010. Demographic data is given in Table 3, and Figure 4 presents the unadjusted patient and graft survival curves by time cohort and KDRI quintile. There was no change in the five-year patient and graft survival probabilities between the time cohorts. Within each time cohort, patient and graft survival was higher at lower KDRIs. Over time there appeared to be a narrowing in the difference in the five-year survival probabilities between the two highest KDRI quintiles due to an improvement in the outcomes from the highest KDRI category.

There was no difference in the unadjusted and adjusted risk of death across transplant cohorts (adjusted hazard ratio, aHR: 1.19, 95%CI: 0.92-1.54 for 2007-2008, and aHR: 1.17, 95%CI: 0.74-1.83 for 2009-2010 compared to 2005-2006, Figure 5). In addition, there was no difference in the unadjusted and adjusted risk of graft failure across transplant cohorts (aHR: 1.22, 95%CI: 0.98-1.50 for 2007-2008, aHR: 1.22, 95%CI: 0.84-1.79 for 2009-2010 compared to 2005-2006, Figure 5). The risk

of death or graft loss in patients transplanted with lower KDRI i.e., better quality, allografts, was lower, however, this effect was reduced when adjusting for recipient and transplant factors (Supplemental Figure 3).

Sensitivity analysis

Complete case analysis yielded similar results to those obtained with the imputed dataset (Supplementary Tables 2, 3 and 4). Analysis of DBD kidneys only revealed slightly lower KDRI scores for each time point but the trend of increasing KDRI scores over time remained (Supplementary Tables 2 and 3).

DISCUSSION

We investigated for trends in the quality of deceased donor kidneys expressed as a standardised KDRI, transplanted between 2005 and 2015, in seven European countries and the effects of these trends on survival outcomes. During this ten-year period, the overall quality of deceased donor kidneys decreased for every subgroup except for recipients aged 18-44 years. The decline in the overall kidney quality was evident as an increase in the standardised KDRI of approximately 1.3% per year, which is in line with changes seen in the US (15). The factors driving these temporal changes were predominantly an increased use of older deceased donors, donors with a prior diagnosis of hypertension or diabetes mellitus and for the Netherlands and the UK the use of DCD donors. As the use of donors with these risk factors varied between countries, we saw that the median standardised KDRI varied between countries. In countries such as the Netherlands and the UK, where in 2015, almost 50% of deceased donors were DCD donors; the standardised KDRI was consistently higher than in Norway, where only 5% of deceased donors were DCD donors. Even with the exclusion of DCD kidneys both the crude and standardised KDRI rose over time. Five-year patient and graft survival probabilities remained unchanged despite the decrease in the overall quality of deceased donor kidneys over time. This could be driven by overall improvements in recipient health,

transplantation procedures and changes in immunosuppressive regimes. Alternatively, it is possible that the quality of deceased donor kidneys does not negatively affect transplantation outcomes in the medium term (of five years), but rather in the long term.

There are several factors which may drive the decline in the quality of deceased donor kidneys over time and which may vary across countries; for example, the demand for deceased donor organ transplantation in terms of the number of patients commencing kidney replacement therapy (KRT); the number of patients listed on the transplant waiting list; and the strength of the living donor transplant programme. It may be that the reduction in the quality of transplanted kidneys, by means of accepting more marginal deceased donors, is an attempt to counterbalance long waiting-times faced by potential transplant recipients. Secondly, the duration and success of the use of marginal donors within a country, is likely to affect the future number of these donors. Additionally, the overall organisational structure of a country's transplantation programme, down to who is responsible for organ procurement may play a contributory role (16). Finally, intercountry differences in KDRI could be influenced by background risk factors within the general population. Within all these countries the prevalence of diabetes mellitus, hypertension and obesity within the general population varies (17) therefore the percentage of potential donors within each country with these features will vary. The increasing prevalence of these diseases (18-20), may well in part explain the trend towards increasing KDRIs.

This study has shown that the poorest quality kidneys are being transplanted into the oldest recipients, this is in keeping with a single-centre German study (9). As we demonstrated; as the age of the recipient increased, the median standardised KDRI increased, whereas with time the youngest recipients received ever better-quality kidneys. It is clear that longevity matching, and therefore utility is appropriately occurring. The distinction between countries with the better and worse quality

kidneys continued, even when stratified by recipient age group, thereby disputing the idea that kidney quality within a country is driven predominantly by recipient qualities.

Despite the decline in the quality of donor kidneys over the past ten years, patient and graft survival remained unchanged. Several factors may have contributed to improving both recipient and graft survival potentially counterbalancing the effects of the decline in the quality of donor kidneys. The risk of recipient death can be decreased, for example, by reducing cardiovascular risk factors. Ceretta et al., demonstrated that between 2005 and 2014 the proportion of Europeans commencing KRT with cardiovascular disease as a comorbidity declined (21). Furthermore Boenink et al., recently showed that the excess mortality risk in Europeans commencing KRT between 2002 and 2015 decreased in relation to the improved survival in the general population (22), in other words the factors resulting in improved KRT outcomes are not limited to overall improvements in the health of the general population. It may be that overall improvements in the relative health of the potential kidney transplant recipient may be paying a role in counterbalancing the effects of the higher KDRI transplant. Though this remains speculative, and to date there is no evidence that individuals are being transplanted in a state of relative improved health. In addition to potential improvement in pre-transplantation health, there is an increased emphasis from transplant groups on the post-transplant control of blood pressure and cardiovascular risk management (23) though again whether this has translated to a decline in post transplantation cardiovascular risk is unclear. Studies specifically assessing trends in the pre-transplantation health of European transplant recipients are needed to determine what is driving this apparent counterbalance in survival outcomes.

One of the factors driving both the increase and country difference in the median standardised KDRI over time was the use of DCD allografts, though it should be emphasised that both the crude and standardised KDRI rose over time even with the exclusion of DCD kidneys. The legal utilisation of DCD donors and the policies relating to their procurement varies considerably

throughout Europe (24). Within the Netherlands and the UK, DCD donors now make up approximately 50% and 42% respectively of the deceased donors (25, 26). Though DCD allografts are typically thought to have worse outcomes than DBD allografts, recent evidence is bringing this into question (27). A Dutch study reported five-year death-censored graft failure for recipients aged <65 years of DBD and DCD allografts from donors aged <65 years of 85.9% (95%CI: 84.1-87.6) and 82.6% (95%CI: 80.2-84.9) respectively (28). Similarly a UK study found equivalent graft outcomes between older controlled DCD and DBD allografts in the same age group (29), though controlled DCD allografts performed less well than DBD allografts with increasing donor and recipient ages, longer CIT times, repeat transplantation, and poor HLA matches (30). Perhaps given the survival improvement from DCD allografts with time, the higher KDRIs seen as a result of the DCD allografts is no longer a true reflection of the donor quality and hence survival is unchanged despite the higher KDRI scores.

Unlike the findings in our study, the median KDRI score in the US has remained fairly low and static between 2005 and 2015 at approximately 1.24 (31). Whereas in 2015, 55% of European deceased kidney donors died of a CVA, 64% were aged over 50 years and 37% were donors after cardiac death, in the US only 25% of kidney donors died of a CVA, 25% were aged over 50 years and only 18% were DCD donors (31) . A recent study by Aubert et al., demonstrated an almost double discard rate in the US as compared to France (32). A lower US discard rate similar to that of France would have resulted in an additional 132,445 allograft life-years. Despite the differences in the distribution of the KDRI score, the 5-year US and European graft survival outcomes remain similar at about 75-85% (31, 33).

The main strength of this study is its ability to compare the trends in the quality of deceased donor kidneys, by means of the standardised KDRI, across seven European countries, within various subgroups over ten years. The KDRI is an easily applicable scoring system; it allows for standardisation and comparison of deceased donor allografts between studies and over time.

However, in the future, in light of improved outcomes of DCD allografts, the inclusion or weighting of DCD donors in the KDRI score may need to be reconsidered. The main limitation of this study is the lack of information regarding organ discard rates and the corresponding KDRI of these organs, therefore we cannot form a complete picture of the potential donor kidneys available over this time period. Correlation with pre-implantation biopsy findings would have been useful though this information was not available. To have a clearer picture we have only included first transplant recipients and so we cannot comment on the donor quality kidney or outcomes of subsequent transplantations. The findings of this study are based on transplants occurring in seven European countries and so we may not be able to generalise these results to the rest of Europe. The relative sizes of the countries/regions in this study are reflected in the findings i.e., the overrepresentation of the UK and large swings in the country specific results from smaller countries/regions. Furthermore, throughout most of Europe, data on ethnicity which is included in the KDRI score is not collected. Given that the prevalence of 'Black or African American' race in the Eurotransplant zone and UK is low (1% in the UK (34)) we assumed all donors where Caucasian. This may have slightly underestimated the KDRI score.

CONCLUSION

Over the past ten years the quality of deceased donor kidneys as expressed by standardised KDRI has decreased across all seven European countries examined by this study, though this did not translate to worse outcomes. A difference in the median kidney quality between countries and between the age groups was seen. As life expectancy in the general population increases, and the prevalence of diabetes mellitus, hypertension and obesity increases it is likely that we will continue to see poorer quality donor kidneys. To avoid this translating into worse transplant outcomes the transplant community should focus on identifying therapies and/or preventative strategies aimed at improving

transplant outcomes despite these lower quality allografts. This approach could further expand the pool of transplantable organs.

CONFLICT OF INTEREST STATEMENT

None declared.

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DATA AVAILABILITY STATEMENT

The data underlying this article cannot be shared with any third party, because the national and regional registries that provided data to the ERA-EDTA Registry remain the owners of the data.

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Box 1 Kidney donor risk index (KDRI) calculation, donor factors and model coefficients as described by Rao et al. (10).

$KDRI_{exp}$ = exp(−0.0194 × I[age<18 yr] × [age−18 yr] + 0.0128 × [age − 40 yr] + 0.0107 × I[age>50 yr] x [age−50 yr] + 0.179 × I[race=African American] + 0.126 × I[hypertensive] + 0.130 × I[diabetes] + 0.220 × [SCr − 1 mg/dl] − 0.209 × I[SCr>1.5 mg/dl] × [SCr − 1.5 mg/dl] + 0.0881× I[cause of death=CVA] − 0.0464 × [/10] − 0.0199 × I[weight<80 kg] × [(weight − 80 kg)/5] + 0.133 × I[donation after cardiac death] + 0.240 × I[hepatitis C]. Where I equates to 1 if the condition is true, and I equates to 0 if the condition is false.

Donor Characteristic	**Applies to:**	**KDRI Coefficient ("Beta")**	**KDRI "XBeta" Component**
Age (integer years)	All donors	0.0128	0.0128*(age-40)
	Donors aged <18 years	-0.0194	-0.0194*(age-18)
	Donors aged >50 years	0.0107	0.0107*(age-50)
Height (cm)	All donors	-0.0464	-0.0464*(hgt-170)/10
Weight (kg)	All donors with weight <80Kg	-0.0199	-0.0199*(wgt-80)/5
Ethnicity	African American donors	0.1790	0.1790
History of hypertension	Hypertensive donors	0.1260	0.1260
History of diabetes mellitus	Diabetic donors	0.1300	0.1300
Cause of death	Donors with cause of death as a cerebrovascular event	0.0881	0.0881
	All donors	0.2200	0.2200*(creat-1.0)
Serum creatinine	Donors with creatinine >1.5 mg/dL	-0.2090	-0.2090*(creat-1.5)
Hepatits C status	Hepatits C positive donors	0.2400	0.2400
Donation after circulatory status	Donation after circulatory death donors	0.1330	0.1330

Table 1. Deceased kidney donor details by year of transplantation, for first kidney only transplants performed between 2005 and 2015, and the average annual percentage change (AAPC) and 95% confidence interval (95%CI) by donor factor, for Austria, Basque Country (Spain), Denmark, the Netherlands, Norway, Slovenia, and the United Kingdom combined. AAPCs with a significance level of less than 0.05 are denoted by an asterix (*). Data contains imputed values.

Year / Donor features	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Average annual percentage change (95% CI)
Number	1865	1837	1852	1927	2082	2204	2255	2417	2560	2593	2585	4.2 (3.5; 4.9)*
Donor age, median (IQR)	50 (38; 59)	50 (39; 59)	52 (39; 60)	51 (40; 60)	52 (41; 61)	53 (43; 63)	55 (43; 64)	55 (45; 64)	54 (43; 65)	55 (44; 65)	55 (44; 65)	1.1 (0.7; 1.4)*
% donors with age <18	6	5	6	5	5	4	4	3	3	3	4	-6.3 (-9.1; -3.5)*
% donors with age > 50	51	51	55	53	56	59	63	63	63	64	64	2.6 (1.9; 3.3)*
Height, cm, median (IQR)	170 (165;180)	170 (165;180)	172 (165;180)	172 (165;180)	170 (165;179)	171 (165;180)	170 (164;179)	171 (165;179)	171 (165;179)	171 (165;179)	171 (164;179)	0.0 (-0.1; 0.1)
Weight, kg, mean (SD)	75 (16.2)	76 (15.6)	76 (16.5)	76 (16.3)	77 (16.7)	78 (17.8)	77 (17.6)	78 (17.3)	78 (18.3)	78 (18.6)	78 (18.5)	0.4 (0.3; 0.5)*
% with BMI >35 kg/m^2	4	4	5	4	6	5	5	6	7	8	7	6.8 (4.1;9.6)*
History of HCV, % yes	0.5	0.1	0.4	0.1	0.2	0.1	0.2	0.1	0.1	0.1	0.2	-11.8 (-20.8; -1.8)*
History of HTN, % yes	23	25	25	26	24	30	32	31	32	31	30	3.2 (1.7, 4.8)*
History of DM, % yes	4	4	5	5	6	6	7	6	7	7	8	6.5 (4.7; 8.4)*
Cause of death; CVA (%)	65	64	64	60	62	65	63	61	57	60	56	-1.2 (-1.9; -0.4)*
Creatinine, mg/dL (IQR)	0.9 (0.7; 1.1)	0.8 (0.7; 1.1)	0.8 (0.6; 1.1)	0.8 (0.6; 1.1)	0.8 (0.6; 1.1)	0.8 (0.6; 1.0)	0.8 (0.6; 1.0)	0.8 (0.6; 1.1)	0.8 (0.6; 1.0)	0.8 (0.6; 1.0)	0.8 (0.6; 1.0)	-0.9 (-0.9; -0.9)*
DCD status, % yes	19	20	23	28	29	29	33	36	38	34	37	6.4 (3.4; 9.5)*

IQR: interquartile range; SD: standard deviation; BMI: body mass index; HCV: hepatitis C status, HTN: hypertension, DM: diabetes mellitus; CVA: cerebrovascular event; DCD: donation after circulatory death; AAPC: average annual percentage change; 95%CI: 95% confidence interval. Data is for Austria, Basque Country (Spain), Denmark, the Netherlands, Norway, Slovenia, and the United Kingdom combined. The average annual percentage change with a significance level of less than 0.05 are denoted by an asterix (*)

Table 2. Deceased donor risk factors as presented in the kidney donor risk index equation, by country/region and for the years 2005, 2010 and 2015.

	Tx year	Austria	Basque Country (Spain)	Denmark	the Netherlands	Norway	Slovenia	United Kingdom
Number of donors	2005	237	102	91	335	104	30	956
	2010	224	101	110	308	136	53	1259
	2015	218	104	126	355	145	54	1573
Donor age, yrs median (IQR)	2005	51 (42; 61)	55 (43; 65)	53 (44; 60)	50 (37; 58)	55 (41; 60.7)	42 (23; 49)	49 (37; 57)
	2010	56 (45; 67)	62 (46; 70)	51 (44; 64)	55 (46; 62)	55 (43.6; 63)	48 (34; 54)	52 (41; 62)
	2015	57 (49; 66)	62 (48; 72)	58 (44; 66)	57 (49; 66)	55 (37; 68)	53 (46; 59)	54 (43; 64)
% of donors <18 years	2005	5	2	6	8	6	23	6
	2010	3	1	4	5	4	15	4
	2015	5	1	6	2	6	4	4
% of donors >50 years	2005	54	66	64	52	63	23	48
	2010	68	67	56	65	62	45	56
	2015	70	70	64	73	61	61	61
Height, cm median (IQR)	2005	175 (168; 180)	165 (160; 175)	170 (165; 180)	174 (168; 180)	175 (165; 180)	170 (165; 175)	170 (163; 178)
	2010	170 (165; 180)	168 (161; 175)	175 (168; 180)	175 (167; 180)	175 (170; 180)	170 (167; 178)	170 (163; 178)
	2015	172 (165; 180)	170 (160; 175)	172 (165; 180)	173 (168; 180)	171 (165; 180)	175 (165; 180)	171 (163; 178)
Weight, kg mean (sd)	2005	80 (16)	73 (13)	75 (17)	74 (15)	80 (21)	69 (23)	74 (16)
	2010	76 (16)	78 (11)	76 (16)	78 (18)	78 (19)	75 (13)	78 (19)
	2015	78 (20)	74 (13)	76 (18)	78 (18)	74 (17)	79 (14)	78 (19)
Donor Diabetes, %	2005	3	3	0	6	8	7	4
	2010	8	9	4	5	4	0	6
%	2015	12	12	2	9	3	9	8
Donor Hypertension %	2005	33	39	27	3	25	20	20
	2010	36	33	31	30	35	38	29
	2015	41	35	33	29	27	30	28
Donor CVA, %	2005	60	56	75	57	54	87	68
	2010	68	70	81	61	61	83	63
	2015	68	65	63	49	67	52	54

Donor creatinine, mg/dL (IQR	2005	0.90 (0.70; 1.12)	0.80 (0.60; 1.00)	0.81 (0.63; 0.97)	0.86 (0.67; 1.05)	0.78 (0.66; 0.88)	0.74 (0.64; 0.90)	0.92 (0.74; 1.15)
	2010	0.80 (0.64; 1.03)	0.74 (0.56; 0.90)	0.68 (0.51; 0.93)	0.77 (0.58; 0.99)	0.73 (0.55; 0.90)	0.90 (0.64; 1.10)	0.83 (0.66; 1.07)
	2015	0.90 (0.68; 1.20)	0.70 (0.58; 0.87)	0.72 (0.59; 1.01)	0.75 (0.59; 0.88)	0.75 (0.58; 1.02)	0.89 (0.70; 1.10)	0.76 (0.59; 1.02)
DCD donor, %	2005	2	0	0	50	0	0	18
	2010	2	2	0	37	0	0	40
	2015	11	21	0	55	5	0	45

Tx: transplantation; IQR: interquartile range; BMI: body mass index; HCV: hepatitis C status, HTN: hypertension, DM: diabetes mellitus; CVA: cerebrovascular event; DCD: donation after circulatory death; SD:standard deviation

Table 3. Baseline characteristics of first, kidney-only transplant recipients by transplant cohort; cohort

1: transplanted during 2005-2006, cohort 2: transplanted during 2007-2008, cohort 3: transplanted during 2009-10.

Characteristics	2005-2006	2007-2008	2009-2010	% missing
Number	3702	3779	4286	
Male, %	62	63	63	0
Age at transplantation, median (IQR)	52 (42; 61)	52 (41; 61)	55 (44; 63)	0
Dialysis time, median (IQR), years	3 (2; 4)	3 (2; 5)	3 (2; 5)	0
Primary kidney disease, %				
Diabetes mellitus type I & II	10	10	12	
Hypertension/renovascular disease	11	12	13	
Glomerulonephritis/sclerosis	21	20	19	
Other	26	26	24	
Missing/unknown	31	32	32	32
Initial KRT modality, %				
Dialysis	79	81	81	
Kidney transplant	12	15	18	
Missing/unknown	9	4	0.7	4
Cold ischaemia time, hours, median (IQR)	17(14; 21)	16 (13; 20)	16 (12; 19)	13
Number of mismatches at HLA-A, B, DR				0.5
0	12	12	11	
1	8	6	5	
2	28	22	21	
3	32	35	37	
4	16	20	20	
5	4	4	4.8	
6	1	1	1.5	
Panel Reactive Antibodies, %				58
0	78	78	77	
>0-10	5	4	5	
10-79	8	9	11	
>79	2	3	2	

IQR: interquartile range; KRT: kidney replacement therapy, HLA: Human leucocyte antigen

Figure legends

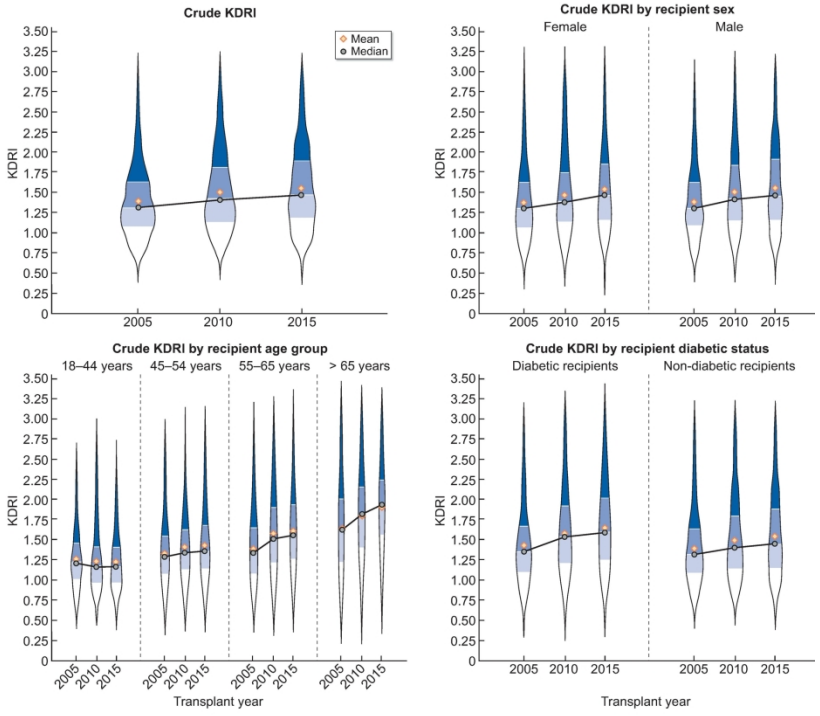
Figure 1. Violin plots of the crude kidney donor risk index (KDRI) for the transplant years 2005, 2010 and 2015 for all countries combined presented; overall (left upper panel), by recipient sex (right upper panel), by recipient age group (left lower panel) and by recipient diabetic status (right lower panel). Black circle indicates median KDRI, and the yellow diamond the mean KDRI.

Figure 2. Standardised median kidney donor risk index (KDRI) and average annual percentage change (AAPC and 95% confidence interval [CI]) during the years 2005 to 2015, for (a) all countries/regions combined and by (b) recipient sex, (c) recipient age group, and (d) recipient diabetic status. The KDRI is scaled relative to the median kidney donor in 2005. AAPCs with a significance level of less than 0.05 are denoted by an asterix (*).

Figure 3. Standardised median kidney donor risk index (KDRI) and average annual percentage change (AAPC and 95% confidence interval [CI]) during the years 2005 to 2015, by country/region. The KDRI is scaled relative to the median kidney donor in 2005 for all countries combined. AAPCs with a significance level of less than 0.05 are denoted by an asterix (*). AT: Austria; ES: Basque Country (Spain); DK: Denmark; NL: Netherlands; NO: Norway; SI: Slovenia; UK: United Kingdom.

Figure 4. Five-year unadjusted patient survival curves for patients aged ≥18 years old receiving their first deceased donor kidney only transplant by (a) time cohort during 2005 and 2010, and by kidney donor risk index (KDRI) quintiles between (b) 2005 and 2006, (c) 2007 and 2008, and (d) 2009 and 2010, in all countries combined and five-year unadjusted graft survival curves by (e) time cohort during 2005 and 2010 and by kidney donor risk index (KDRI) quintiles between (f) 2005 and 2006, (g) 2007 and 2008, and (h) 2009 and 2010 for all countries/regions combined.

Figure 5. Five-year risk and 95% confidence interval of unadjusted and adjusted death and five-year risk of unadjusted and adjusted graft failure by time cohort; 2005-2006; 2007-2008; 2009-2010, for all countries/regions combined. Adjustments made for recipient age at transplantation, recipient sex, primary kidney disease, cold ischaemia time, human leukocyte antigen mismatch score, and the country of transplantation.



NDT-02168-2020.R1-fig1

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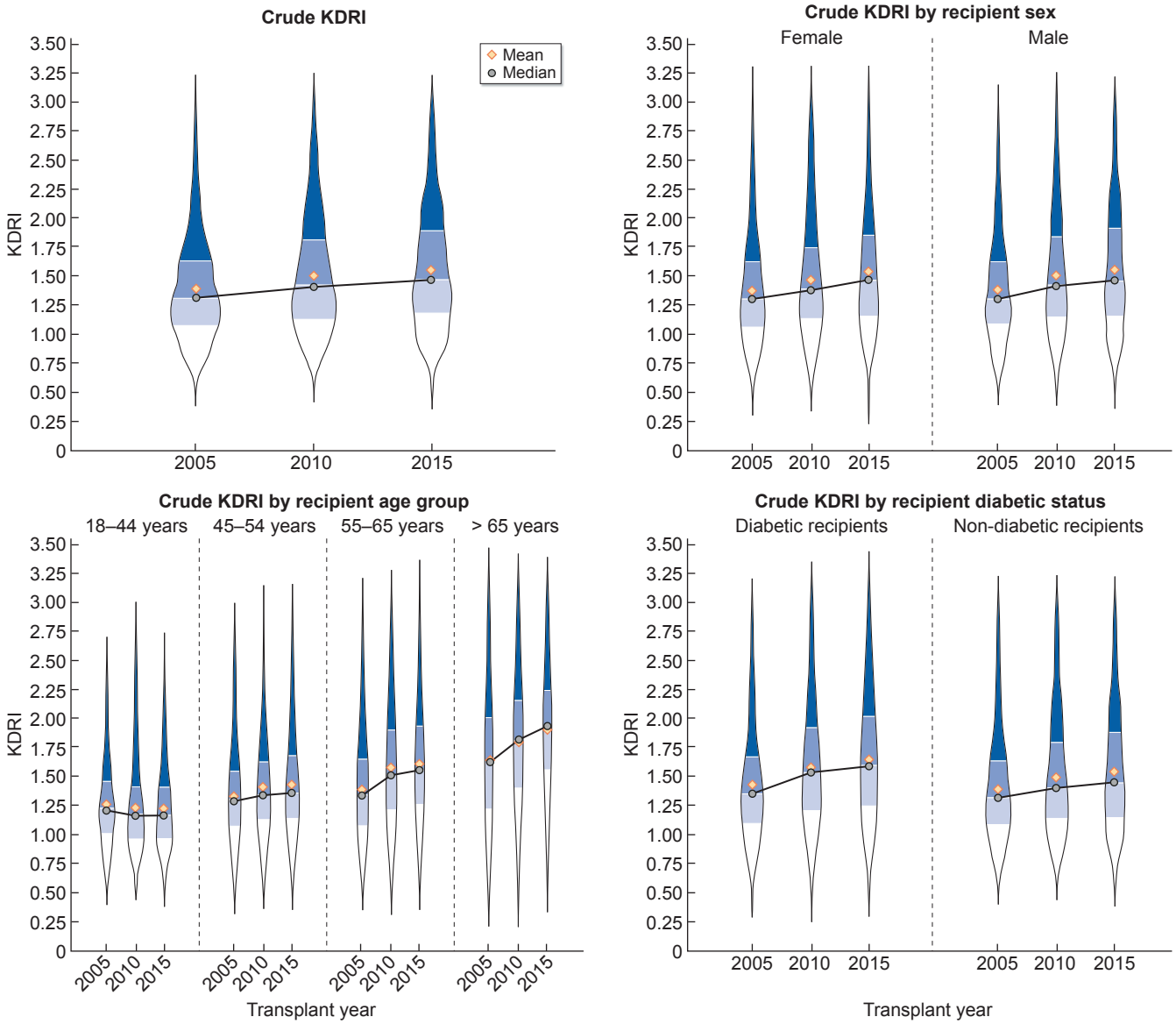
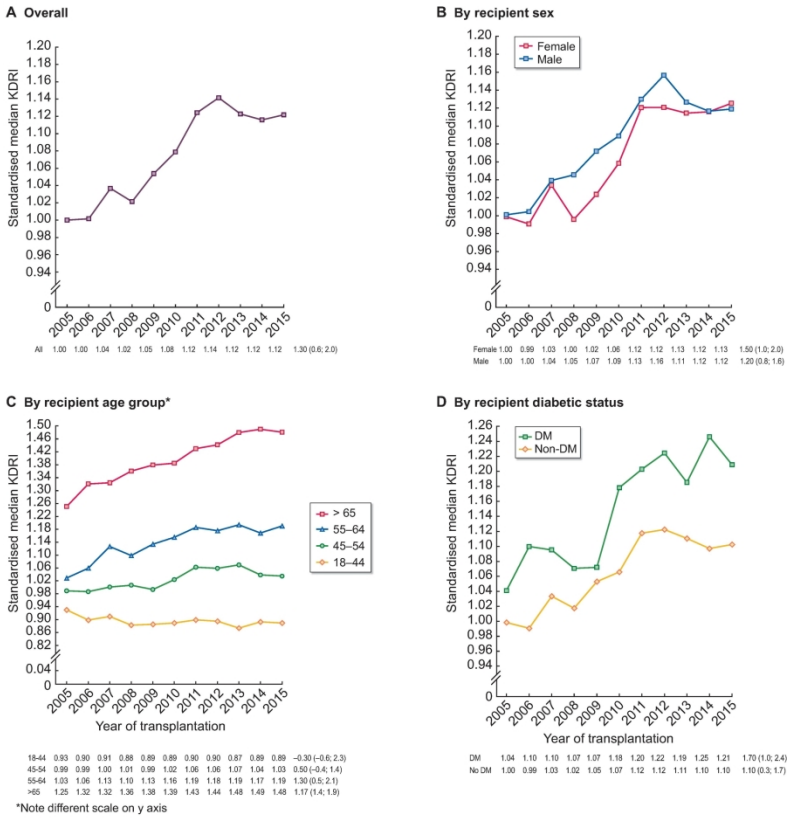


NDT-02168-2020.R1-fig1



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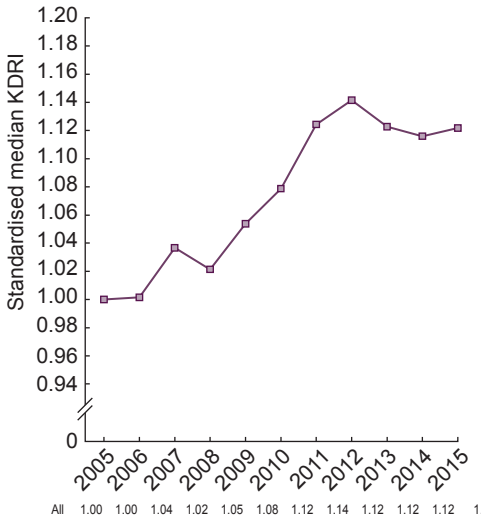
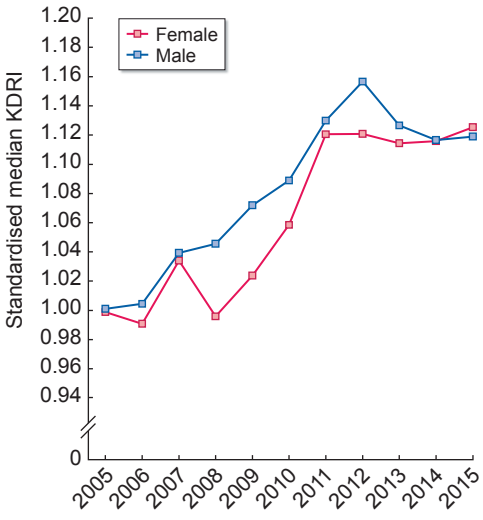
A Overall



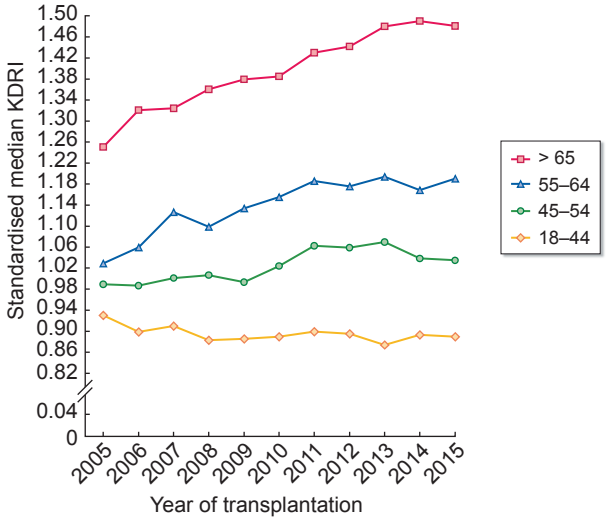
All	1.00	1.00	1.04	1.02	1.05	1.08	1.12	1.14	1.12	1.12	1.12	1.30 (0.6; 2.0)

B By recipient sex



Female	1.00	0.99	1.03	1.00	1.02	1.06	1.12	1.12	1.13	1.12	1.13	1.50 (1.0; 2.0)
Male	1.00	1.00	1.04	1.05	1.07	1.09	1.13	1.16	1.11	1.12	1.12	1.20 (0.8; 1.6)

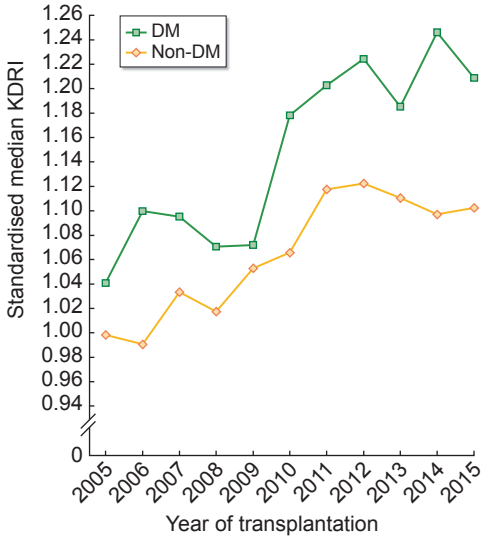
C By recipient age group*



18-44	0.93	0.90	0.91	0.88	0.89	0.89	0.90	0.90	0.87	0.89	0.89	−0.30 (−0.6; 2.3)
45-54	0.99	0.99	1.00	1.01	0.99	1.02	1.06	1.06	1.07	1.04	1.03	0.50 (−0.4; 1.4)
55-64	1.03	1.06	1.13	1.10	1.13	1.16	1.19	1.18	1.19	1.17	1.19	1.30 (0.5; 2.1)
>65	1.25	1.32	1.32	1.36	1.38	1.39	1.43	1.44	1.48	1.49	1.48	1.17 (1.4; 1.9)

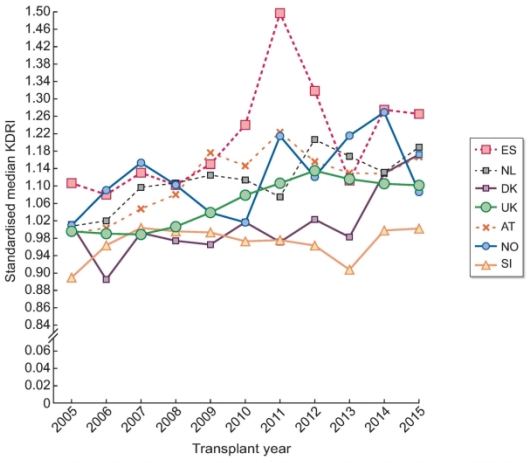
*Note different scale on y axis

D By recipient diabetic status



DM	1.04	1.10	1.10	1.07	1.07	1.18	1.20	1.22	1.19	1.25	1.21	1.70 (1.0; 2.4)
No DM	1.00	0.99	1.03	1.02	1.05	1.07	1.12	1.12	1.11	1.10	1.10	1.10 (0.3; 1.7)

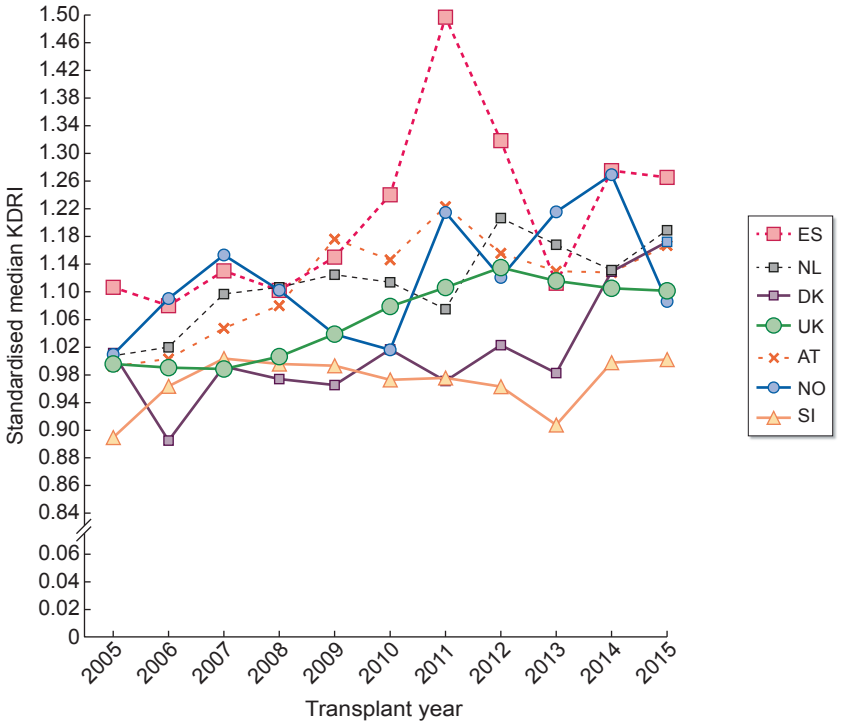
NDT-02168-2020.R1-fig2



AT	0.99	1.00	1.05	1.08	1.18	1.15	1.22	1.16	1.13	1.13	1.17	1.40 (0.3; 2.5)
ES	1.11	1.08	1.13	1.10	1.15	1.24	1.50	1.32	1.11	1.28	1.27	1.80 (–0.2; 3.9)
DK	1.01	0.89	0.99	0.97	0.97	1.02	0.97	1.02	0.98	1.13	1.17	1.70 (0.5; 2.9)
NL	1.01	1.02	1.10	1.11	1.12	1.11	1.08	1.21	1.17	1.13	1.19	1.40 (0.7; 2.2)
NO	1.01	1.09	1.15	1.10	1.04	1.02	1.21	1.12	1.22	1.27	1.09	1.20 (–0.2; 2.7)
SI	0.89	0.96	1.00	1.00	0.99	0.97	0.98	0.96	0.91	1.00	1.00	0.30 (–0.6;1.2)
UK	1.00	0.99	0.99	1.01	1.14	1.08	1.11	1.14	1.12	1.11	1.10	1.30 (0.4;2.2)

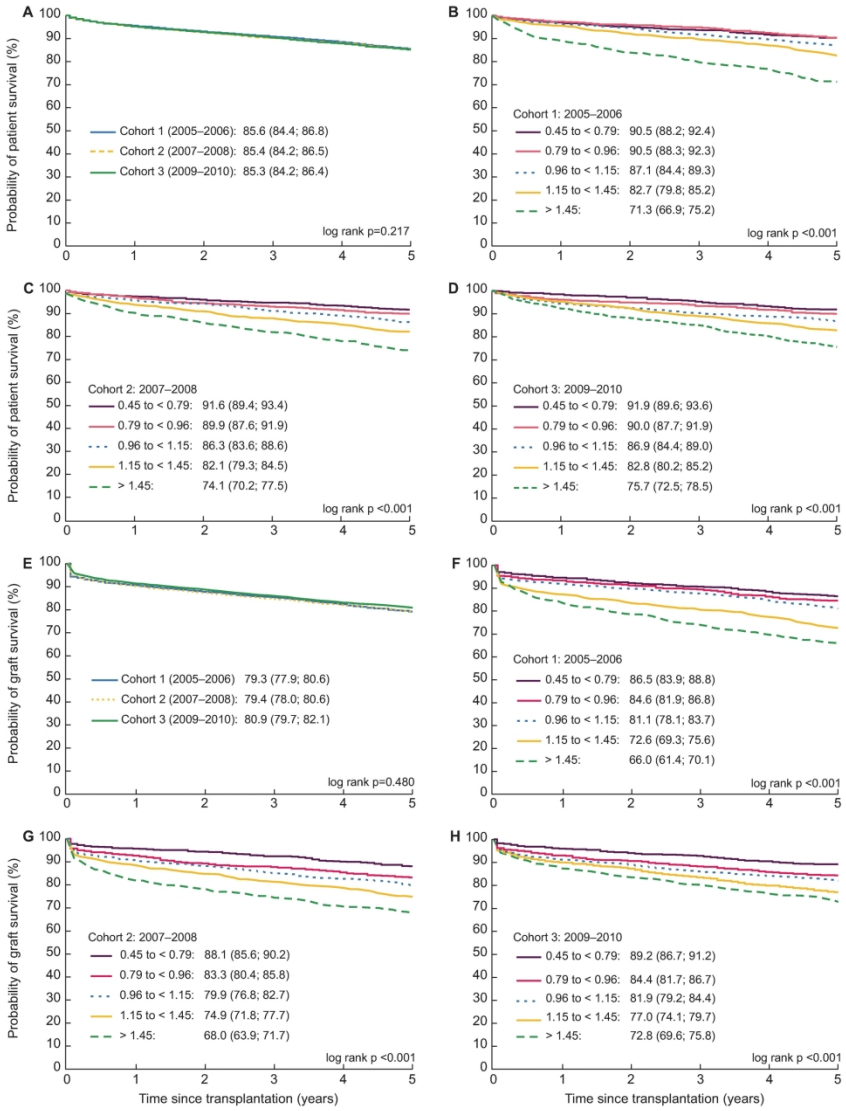
NDT-02168-2020.R1-fig3

162x252mm (300 x 300 DPI)



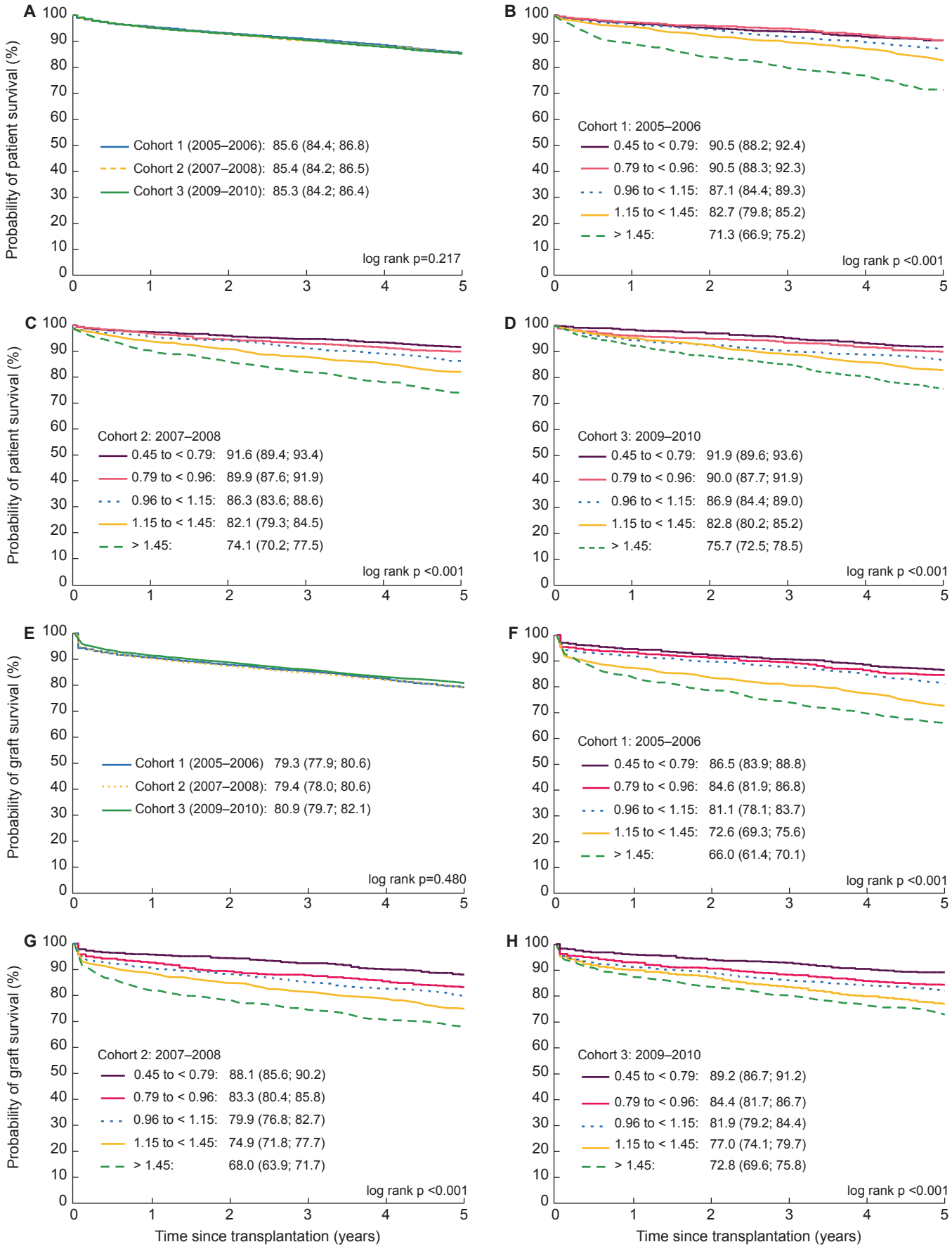
AT	0.99	1.00	1.05	1.08	1.18	1.15	1.22	1.16	1.13	1.13	1.17	1.40 (0.3; 2.5)
ES	1.11	1.08	1.13	1.10	1.15	1.24	1.50	1.32	1.11	1.28	1.27	1.80 (–0.2; 3.9)
DK	1.01	0.89	0.99	0.97	0.97	1.02	0.97	1.02	0.98	1.13	1.17	1.70 (0.5; 2.9)
NL	1.01	1.02	1.10	1.11	1.12	1.11	1.08	1.21	1.17	1.13	1.19	1.40 (0.7; 2.2)
NO	1.01	1.09	1.15	1.10	1.04	1.02	1.21	1.12	1.22	1.27	1.09	1.20 (–0.2; 2.7)
SI	0.89	0.96	1.00	1.00	0.99	0.97	0.98	0.96	0.91	1.00	1.00	0.30 (–0.6;1.2)
UK	1.00	0.99	0.99	1.01	1.14	1.08	1.11	1.14	1.12	1.11	1.10	1.30 (0.4;2.2)

NDT-02168-2020.R1-fig3

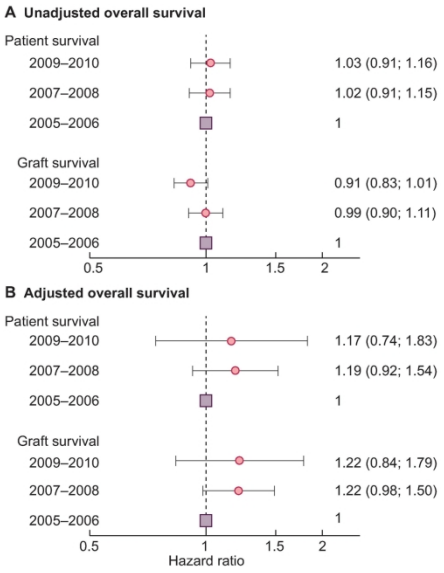


NDT-02168-2020.R1-fig4

178x254mm (300 x 300 DPI)

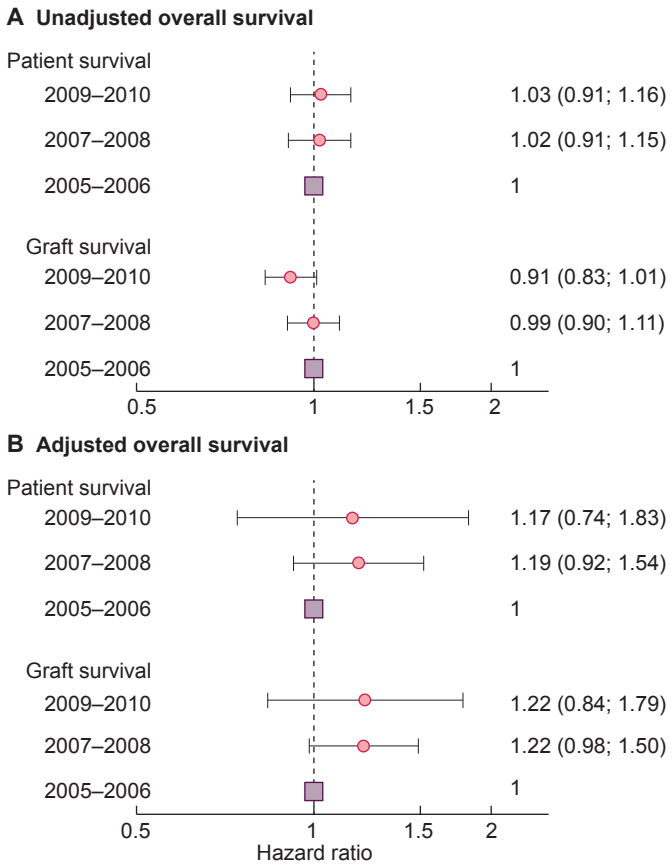


NDT-02168-2020.R1-fig4



NDT-02168-2020.R1-fig5

88x241mm (300 x 300 DPI)



NDT-02168-2020.R1-fig5